DATE: 10/24/2001

OIPE

TIME: 15:12:30 PATENT APPLICATION: US/09/903,216 Input Set : A:\Rih32d21.app Output Set: N:\CRF3\10242001\1903216.raw 3 <110> APPLICANT: Wands, Jack R. de la Monte, Suzanne M. Ince, Nedim Carlson, Rolf I.

8 <120> TITLE OF INVENTION: DIAGNOSIS AND TREATMENT OF MALIGNANT NEOPLASMS

0 <130> FILE REFERENCE: 21486-032 DIV2 Carlson, Rolf I. 10 <130> FILE REFERENCE: 21486-032 DIV2 12 <140> CURRENT APPLICATION NUMBER: 09/903,216 13 <141> CURRENT FILING DATE: 2001-07-11 15 <150> PRIOR APPLICATION NUMBER: 09/436,184 16 <151> PRIOR FILING DATE: 1999-11-08

18 <160> NUMBER OF SEQ ID NOS: 9 20 <170> SOFTWARE: PatentIn Ver. 2.1 22 <210> SEQ ID NO: 1 23 <211> LENGTH: 36 24 <212> TYPE: PRT 25 <213> ORGANISM: Artificial Sequence 27 <220> FEATURE: 28 <223> OTHER INFORMATION: Description of Artificial Sequence: Consensus EGF-like domain 31 <220> FEATURE: 32 <221> NAME/KEY: VARIANT 33 <222> LOCATION: (2)..(8) 34 <223> OTHER INFORMATION: Wherein Xaa is any amino acid 36 <220> FEATURE: 37 <221> NAME/KEY: VARIANT 38 <222> LOCATION: (10)..(13) 39 <223> OTHER INFORMATION: Wherein Xaa is any amino acid. 41 <220> FEATURE: 42 <221> NAME/KEY: VARIANT 43 <222> LOCATION: (15)..(24) 44 <223> OTHER INFORMATION: Wherein Xaa is any amino acid. 46 <220> FEATURE: 47 <221> NAME/KEY: VARIANT 48 <222> LOCATION: (26) 49 <223> OTHER INFORMATION: Wherein Xaa is any amino acid. 51 <220> FEATURE: 52 <221> NAME/KEY: VARIANT 53 <222> LOCATION: (28)..(35) 54 <223> OTHER INFORMATION: Wherein Xaa is any amino acid. 56 <400> SEQUENCE: 1 --> 57 Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Cys (Xaa Xaa -> 60 Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys (Xaa Cys Xaa Xaa Xaa Xaa 61 25 W--> 63(Xaa Xaa Xaa Cys 35 64 67 <210> SEQ ID NO: 2

RAW SEQUENCE LISTING

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Input Set : A:\Rih32d21.app

Output Set: N:\CRF3\10242001\I903216.raw

68 <211> LENGTH: 758 69 <212> TYPE: PRT 70 <213> ORGANISM: Homo sapiens 72 <400> SEQUENCE: 2 73 Met Ala Gln Arg Lys Asn Ala Lys Ser Ser Gly Asn Ser Ser Ser Ser 76 Gly Ser Gly Ser Gly Ser Thr Ser Ala Gly Ser Ser Pro Gly Ala 79 Arg Arg Glu Thr Lys His Gly Gly His Lys Asn Gly Arg Lys Gly Gly 40 82 Leu Ser Gly Thr Ser Phe Phe Thr Trp Phe Met Val Ile Ala Leu Leu 85 Gly Val Trp Thr Ser Val Ala Val Val Trp Phe Asp Leu Val Asp Tyr 88 Glu Glu Val Leu Gly Lys Leu Gly Ile Tyr Asp Ala Asp Gly Asp Gly 91 Asp Phe Asp Val Asp Asp Ala Lys Val Leu Leu Gly Leu Lys Glu Arg 100 105 94 Ser Thr Ser Glu Pro Ala Val Pro Pro Glu Glu Ala Glu Pro His Thr 120 97 Glu Pro Glu Glu Gln Val Pro Val Glu Ala Glu Pro Gln Asn Ile Glu 100 Asp Glu Ala Lys Glu Gln Ile Gln Ser Leu Leu His Glu Met Val His 150 155 103 Ala Glu His Val Glu Gly Glu Asp Leu Gln Glu Asp Gly Pro Thr 165 170 106 Gly Glu Pro Gln Glu Asp Asp Glu Phe Leu Met Ala Thr Asp Val 180 185 190 109 Asp Asp Arg Phe Glu Thr Leu Glu Pro Glu Val Ser His Glu Glu Thr 195 200 112 Glu His Ser Tyr His Val Glu Glu Thr Val Ser Gln Asp Cys Asn Gln 215 115 Asp Met Glu Glu Met Met Ser Glu Gln Glu Asn Pro Asp Ser Ser Glu 235 118 Pro Val Val Glu Asp Glu Arg Leu His His Asp Thr Asp Asp Val Thr 245 121 Tyr Gln Val Tyr Glu Glu Gln Ala Val Tyr Glu Pro Leu Glu Asn Glu 260 265 124 Gly Ile Glu Ile Thr Glu Val Thr Ala Pro Pro Glu Asp Asn Pro Val 280 127 Glu Asp Ser Gln Val Ile Val Glu Glu Val Ser Ile Phe Pro Val Glu 300 290 295 130 Glu Gln Gln Glu Val Pro Pro Glu Thr Asn Arg Lys Thr Asp Asp Pro 310 315 133 Glu Gln Lys Ala Lys Val Lys Lys Lys Pro Lys Leu Leu Asn Lys 325 330 136 Phe Asp Lys Thr Ile Lys Ala Glu Leu Asp Ala Ala Glu Lys Leu Arg 345 139 Lys Arg Gly Lys Ile Glu Glu Ala Val Asn Ala Phe Lys Glu Leu Val

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Input Set : A:\Rih32d21.app

Output Set: N:\CRF3\10242001\I903216.raw

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145	Glu	Asp	Asp	Leu	Ala	Glu	Lys	Arg	Arg	Ser	Asn	Glu	Val	Leu	Arg	Gly
	385					390					395					400
148	Ala	Ile	Glu	Thr	Tyr	Gln	Glu	Val	Ala	Ser	Leu	Pro	Asp	Val	Pro	Ala
149					405					410			_		415	
151	Asp	Leu	Leu	Lys	Leu	Ser	Leu	Lys	Arg	Arg	Ser	Asp	Arg	Gln	Gln	Phe
152				420					425			_		430		
154	Leu	Gly	His	Met	Arg	Gly	Ser	Leu	Leu	Thr	Leu	Gln	Arg	Leu	Val	Gln
155			435					440					445			
157	Leu	Phe	Pro	Asn	Asp	Thr	Ser	Leu	Lys	Asn	Asp	Leu	Gly	Val	Gly	Tyr
158		450					455				_	460				
160	Leu	Leu	Ile	Gly	Asp	Asn	Asp	Asn	Ala	Lys	Lys	Val	Tyr	Glu	Glu	Val
	465					470					475					480
163	Leu	Ser	Val	Thr	Pro	Asn	Asp	Gly	Phe	Ala	Lys	Val	His	Tyr	Gly	Phe
164					485					490					495	
166	Ile	Leu	Lys	Ala	Gln	Asn	Lys	Ile	Ala	Glu	Ser	Ile	Pro	Tyr	Leu	Lys
167				500					505					510		
169	Glu	Gly	Ile	Glu	Ser	Gly	Asp	Pro	Gly	Thr	Asp	Asp	Gly	Arg	Phe	Tyr
170			515					520					525			
172	Phe	His	Leu	Gly	Asp	Ala	Met	Gln	Arg	Val	Gly	Asn	Lys	Glu	Ala	Tyr
173		530					535					540				
175	Lys	Trp	Tyr	Glu	Leu	Gly	His	Lys	Arg	Gly	His	Phe	Ala	Ser	Val	Trp
176	545					550					555					560
178	Gln	Arg	Ser	Leu	\mathtt{Tyr}	Asn	Val	Asn	Gly	Leu	Lys	Ala	Gln	Pro	Trp	Trp
179					565					570			•		575	
181	Thr	Pro	Lys	Glu	Thr	Gly	Tyr	Thr		Leu	Val	Lys	Ser		Glu	Arg
182				580					585					590		
184	Asn	\mathtt{Trp}		Leu	Ile	Arg	Asp		Gly	Leu	Ala	Val	Met	Asp	Lys	Ala
185			595					600					605			
			Leu	Phe	Leu	Pro		Asp	Glu	Asn	Leu		Glu	Lys	Gly	Asp
188		610		_			615		_	_		620		_		_
	_	Ser	Gln	Phe	Thr		Trp	Gln	Gln	Gly	Arg	Arg	Asn	Glu	Asn	
	625					630		_		_	635		_		_	640
	Cys	Lys	GïÀ	Ala		Lys	Thr	Cys	Thr		Leu	Glu	Lys	Phe		GIu
194	_,	_,	_,	_	645	_			_,	650	_	_			655	_
	Thr	Thr	GLY	_	Arg	Arg	GLY	GIn		Lys	Tyr	ser	ITe		His	Pro
197	a 1	1	·	660		_	'		665		m1	•	~	670	.	•
	GLŸ	Thr		Val	Trp	Pro	Hls		GLY	Pro	Thr	Asn		Arg	Leu	Arg
200		•	675		_			680	_	~ 1	~1	•	685	+1 .	_	
	Met		Leu	GIY	Leu	Val		Pro	Lys	GLu	Gly		Lys	IIe	Arg	Cys
203		690		1	_		695			-1	_	700	_			_
		Asn	GLu	Thr	Arg		Trp	GLU	GIU	Gly	Lys	Val	Leu	тте	Pne	
	705	~	Dl	0.1	TT 2 .	710	*** *	m-··	a 2 -	3	715	G		D1	3	720
	Asp	ser	ьиe	GLu		Glu	val	ттр	GIN		АТа	ser	ser	hue	-	Leu
209	T1 -	Db -	T 1 -	17- 1	725	17- 3	m	TT 2	D	730	T ~	m 1	D	~ 1	735	3
	тте	Fue	тте		ASP	val	ırp	HIS		GIU	Leu	THE	PLO		GIN	arg
212				7.40					745	•				750		

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Input Set : A:\Rih32d21.app

Output Set: N:\CRF3\10242001\1903216.raw

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215
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226 agcatggagg acacaagaat gggaggaaag gcggactctc gggaacttca ttcttcacgt 180
227 ggtttatggt gattgcattg ctgggcgtct ggacatctgt agctgtcgtt tggtttgatc 240
228 ttgttgacta tgaggaagtt ctaggaaaac taggaatcta tgatgctgat ggtgatggag 300
229 attttgatgt ggatgatgcc aaagttttat taggacttaa agagagatct acttcagagc 360
230 cagcagtece gecagaagag getgageeac acaetgagee egaggageag gtteetgtgg 420
231 aggcagaacc ccagaatatc gaagatgaag caaaagaaca aattcagtcc cttctccatg 480
232 aaatggtaca cgcagaacat gttgagggag aagacttgca acaagaagat ggacccacag 540
233 gagaaccaca acaagaggat gatgagtttc ttatggcgac tgatgtagat gatagatttg 600
234 agaccctgga acctgaagta tctcatgaag aaaccgagca tagttaccac gtggaagaga 660
235 cagtttcaca agactgtaat caggatatgg aagagatgat gtctgagcag gaaaatccag 720
236 attccagtga accagtagta gaaqatgaaa gattgcacca tgatacagat gatgtaacat 780
237 accaagtcta tgaggaacaa gcagtatatg aacctctaga aaatgaaggg atagaaatca 840
238 cagaagtaac tgctcccct gaggataatc ctgtagaaga ttcacaggta attgtagaag 900
239 aagtaagcat ttttcctgtg gaagaacagc aggaagtacc accagaaaca aatagaaaaa 960
240 cagatgatee agaacaaaaa gcaaaagtta agaaaaagaa geetaaaett ttaaataaat 1020
241 ttgataagac tattaaagct gaacttgatg ctgcagaaaa actccgtaaa aggggaaaaa 1080
242 ttgaggaage agtgaatgea tttaaagaae tagtaegeaa ataeeeteag agteeaegag 1140
243 caaqatatqq qaaqqcqcaq tqtqaqqatq atttqqctqa qaaqaqqaqa agtaatqagg 1200
244 tgctacgtgg agccatcgag acctaccaag aggtggccag cctacctgat gtccctgcag 1260
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249 teetgaagge acagaacaaa attgetgaga geateecata tttaaaggaa ggaatagaat 1560
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256 atgaaaatgo otgoaaagga gotootaaaa ootgtacott actagaaaag ttooocgaga 1980
257 caacaggatg cagaagagga cagatcaaat attccatcat gcaccccggg actcacgtgt 2040
258 ggccgcacac agggcccaca aactgcaggc tccgaatgca cctgggcttg gtgattccca 2100
259 aggaaggetg caagattega tgtgecaaeg agaceaggae etgggaggaa ggeaaggtge 2160
260 tcatctttga tgactccttt gagcacgagg tatggcagga tgcctcatct ttccggctga 2220
261 tattcatcgt ggatgtgtgg catccggaac tgacaccaca gcagagacgc agccttccag 2280
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265 <210> SEQ ID NO: 4
266 <211> LENGTH: 31
267 <212> TYPE: PRT
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Input Set : A:\Rih32d21.app

Output Set: N:\CRF3\10242001\1903216.raw

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     276 <222> LOCATION: (3)..(5)
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     299 <221> NAME/KEY: VARIANT
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     319 <213> ORGANISM: Homo sapiens
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     326
     328 Arg Ala Ala Ser Glu Ala Gly Gly Pro Ala Arg Leu Glu Tyr Tyr Glu
                                      40
     331 Asn Glu Lys Lys Trp Arg His Lys Ser Ser Ala Pro Lys Arg Ser Ile
     332
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VERIFICATION SUMMARY

DATE: 10/24/2001

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TIME: 15:12:31 .

Input Set : A:\Rih32d21.app

Output Set: N:\CRF3\10242001\1903216.raw

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